

REMARKS

Reconsideration and allowance of this application are respectfully requested in light of the following remarks.

Claim Status

Claims 1-20 were presented in the originally filed application. Claims 14-20 are withdrawn. Claims 1 and 13 are amended. Claims 3 and 7 were cancelled. Claims 1, 2, 4-6 and 8-13 are pending. No new matter was added.

Discussion

Claims 1-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 6,582,941 (Yokochi), U.S. Patent No. 6,509,178 (Tanaka), EP 0 113 183 (Carson), and Bajpai. Applicant traverses.

It appears from the Examiner's comments that the novelty of the instant invention is not in question. The Examiner does however question the inventive step of this instant invention. Applicant believes that the Examiner's inventive step objections are incorrect as these objections appear to be based on an improper ex-post facto analysis of the instant invention and fail to consider the advantages and effects achieved by the invention, most particularly the improved DHA space-time yields

which are clearly demonstrated in Examples 1 through 5 within the instant specification. The Examiner reasons that the advantages and effects of the instant invention need not be considered because (1) the instant invention is directed to culturing microorganisms of the genus *Thraustochytriales*, and (2) the instant invention does not require the recovery of the products which result from the culturing.

Applicant has further clarified the instant invention by amending independent claims 1 and 13 to require the isolation of PUFAs from the microorganisms and/or the fermentation medium (Specification, Page 3, Lines 25-29) wherein the microorganisms bring forth a production of more than 10 wt% docosahexaenoic acid (DHA) per unit of weight of dry biomass. (Specification, Page 4, Lines 4-6). Amended claims 1 and 13 also require the pH value of said fermentation medium being adjusted to within the range of 5 to 7 prior to the start of fermentation (claim 13) by adding a corresponding acid or base (claim 1). (Specification, Page 8, Lines 26-28). The isolation of PUFAs from the microorganisms and/or the fermentation medium overcomes the Examiner's second objection above. The requirement that the microorganisms bring forth a production of more than 10 wt% docosahexaenoic acid (DHA) per unit of weight of dry biomass clarifies that high DHA yields are achieved by the instant

invention as is clearly demonstrated in Examples 1.1, 1.2 and 1.3 within the instant Specification. The pH range of 5 to 7 further delimits the cited prior art, most specifically Yokochi and Tanaka which, despite the passive reference of a broader pH range in the general description, each disclose in their Examples starting pH ranges which are much lower than that of the instant invention. (See Yokochi Examples 5 and 10 and Tanaka Examples 1 and 2).

Additionally, the advantages and effects achieved by the use of CaCO_3 in the instant invention are clearly demonstrated in Example 4. More specifically, Table 4 shows the advantages of producing PUFA by comparing PUFA production in a culture medium which is stabilized by CaCO_3 with a medium which is not stabilized by CaCO_3 . Table 4 clearly demonstrates that both the starting pH value must be met and that CaCO_3 must be used in order to achieve the improved DHA space-time yields of the instant invention. (The significant increase in the DHA space-time yield of more than 15% for CaCO_3 -buffered fermentation compared to pH-controlled fermentation.)

Newly amended claims 1 and 13 now clearly demonstrate that the combination of Yokochi, Tanaka, Carson, and Bajpai fail to

establish a *prima facie* case of obviousness. MPEP §2143 "Basic Requirements of a *Prima Facie* Case of Obviousness" states:

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine references teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all claim limitations.

Regarding the third criterion, the court has stated that "to establish *prima facie* obviousness of a claimed invention, **all** the claim limitations must be taught or suggested by the prior art." *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974).

Applicant contends that none of the prior art references, Yokochi, Tanaka, Carson, and Bajpai, alone or in combination, teach, suggest, or provide a motivation for making an article of manufacture with all of the claim elements from independent claims 1 and 13. More specifically, Applicant contends that none of the prior art references, alone or in combination, teach, suggest or provide a motivation for a method for cultivating microorganisms of the order *Thraustochytriales*, comprising the steps of: cultivating the microorganisms in a fermentation medium containing CaCO_3 as an essential (or exclusive) means for pH value stabilization, where content of CaCO_3 , in the fermentation medium is 3 to 15 g/l; adjusting the

pH value of the fermentation medium to the range of 5 to 7 prior to the start of fermentation by adding a corresponding acid or base followed by isolating PUFAs from the microorganisms and/or the fermentation medium wherein the microorganisms bring forth a production of more than 10 wt% docosahexaenoic acid (DHA) per unit of weight of dry biomass.

In sum, the rejection goes like this: Yokochi is cited for the purpose of disclosing cultivation of *Schizochytrium* Genus SR21 for the production of DHA and DPA. (Yokochi, Column 18, Lines 14-23). As noted by the Examiner, Yokochi makes no reference to the use of calcium carbonate as a material for the adjustment of pH levels in the fermentation medium. The Examiner then cites Tanaka for the purpose of disclosing cultivation of *Ulenia* sp. strain SAM 2179 for the production of DHA and DPA. (Tanaka, Column 2, Lines 63-65). As noted by the Examiner, Tanaka makes no reference to the use of calcium carbonate as a material for the adjustment of pH levels in the fermentation medium. The Examiner then cites Carson as disclosing the use of calcium carbonate in the liquid phase of a fermentation mixture. (Carson, Page 9, Lines 7-11). The Examiner also cites the reference by Bajpai as disclosing the cultivation of *Thraustochytrium aureum*, in a culture medium containing calcium carbonate.

The deficiencies of Tanaka, Yokochi, Bajpai and EP 0 113 183 (Carson) were thoroughly discussed in the previous office action which is herein incorporated by reference. In summary, Bajpai clearly teaches that the pH value does not have to be kept within a range of 5-7, but instead is permitted to decrease far below pH 6 during cultivation. Consequently, Bajpai et al does not suggest or even hint at the cultivation of Thraustochytriales in the presence of 3 - 15 g/L calcium carbonate as the essential means for pH value stabilization followed by isolating PUFAs from the microorganisms and/or the fermentation medium wherein the microorganisms bring forth a production of more than 10 wt% docosahexaenoic acid (DHA) per unit of weight of dry biomass. Additionally in Table 1, Bajpai clearly discloses very low DHA space-time yields. (DHA in biomass / biomass * 24 h/d/40h << 0.050mg/L. These low DHA space-time yields make it patently obvious that a person skilled in the art would never consider this document in order to solve the underlying problem solved by the instant invention.

It must be noted that Carson does not describe, mention, or even hint at space-time yields. Based on this fact, a person skilled in the art would never consider this document in order to solve the underlying problem solved by the instant invention.

Additionally, it must be reiterated that yeasts, as used for alcoholic fermentation on the one hand and Thraustochytriales on the other hand, are totally different organisms. It must also be noted that the process of alcoholic fermentation (in which carbohydrates are metabolized to ethanol and CO₂) is totally different from the production of polyunsaturated fatty acids (PUFAs). Therefore, from the view of an individual who is skilled in the art, it is inappropriate and inconceivable that based on the cultivation conditions disclosed in Carson, conclusions may be drawn with respect to the optimization of a completely different metabolic process in a completely different organism. A person skill in the art would know that studies on the fermentation of yeasts, such as that described in Carson, cannot and do not provide a solution to the above problem based on the simple fact that different metabolic processes occur in yeasts.

As stated in the previous office action, the prior art reference or combination of references relied upon by the Examiner must teach or suggest all of the limitations of the claims. See *In re Zurko*, 111 F.3d 887, 888-89, 42 U.S.P.Q.2d 1467, 1478 (Fed. Cir. 1997); *In re Wilson*, 424 F.2d 1382, 1385, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970) ("All words in a claim must be considered in judging the patentability of that claim

against the prior art."). The teachings or suggestions, as well as the expectation of success, must come from the prior art, not applicant's disclosure. See *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). In this instance, from the information detailed above, it is clear that Yokochi, Tanaka, Carson, and Bajpai fail to teach or suggest all the limitations of Applicant's claims.

Hindsight reconstruction is not permitted as the Federal Circuit has repeatedly warned that the requisite motivation to modify a reference must come from the prior art, not Applicant's specification. See *In re Dow Chem. Co.*, 837 F.2d 469, 473, 5 U.S.P.Q.2d 1529, 1531-32 (Fed. Cir. 1988) ("there must be a reason or suggestion in the art for selecting the procedure used, other than the knowledge learned from the applicant's disclosure.") Using an Applicant's disclosure as a blueprint to reconstruct the claimed invention from isolated piece of the prior art contravenes the statutory mandate of section 103 of judging obviousness at the point in time when the invention was made. See *Grain Processing Corp. v. American Maize-Prods. Co.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988).


Only hindsight reconstruction based upon the instant specification would lead the Examiner to the conclusion that the

claims in the instant application are rejected under §103 as unpatentable over Yokochi, Tanaka, Carson, and Bajpai. Accordingly, the instant rejection of independent claims 1 and 13 must be removed.

In reference to claims 2, 4-6 and 8-12, dependent claims are nonobvious under section 103 if the independent claims from which they depend are nonobvious. *Hartness Int'l, Inc. v. Simplimatic Eng'g Co.*, 819 F.2d 1100, 1108, 2 USPQ2d 1826, 1831 (Fed. Cir. 1987); *In re Abele*, 684 F.2d 902, 910, 214 USPQ 682, 689 (CCPA 1982); see also *In re Sernaker*, 702 F.2d 989, 991, 217 USPQ 1, 3 (Fed. Cir. 1983). Thus, claims 2, 4-6 and 8-12 are not unpatentable over Yokochi, Tanaka, Carson, and Bajpai and should be allowed.

Reconsideration and allowance of this application is respectfully requested.

Respectfully submitted,



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